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Six Hundred Fifty-Six Consecutive Explorations for Primary Hyperparathyroidism

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Objective

To review the outcomes of 656 consecutive parathyroid explorations performed by a single surgeon and to compare the results of conventional and minimally invasive parathyroidectomy (MIP) techniques.

Summary Background Data

Traditional surgery for primary hyperparathyroidism (HPTH) involves bilateral cervical exploration, which is usually accomplished under general endotracheal anesthesia. The MIP technique involves preoperative localization with sestamibi scans, surgeon-administered cervical block anesthesia, directed exploration through a small incision, intraoperative rapid parathyroid hormone assay, and discharge within 2 to 3 hours of surgery.

Methods

Six hundred fifty-six consecutive patients with primary HPTH underwent exploration between January 1990 and March 2001.

Results

MIP was used with ever-increasing frequency beginning in March 1998. Four hundred one procedures (61%) were performed using the standard technique and 255 patients (39%) were selected for MIP. The success rate for the entire series was 98%, with no significant differences comparing traditional and MIP techniques. The overall complication rate of 2.3% reflects 3.0% and 1.2% rates in the standard and MIP groups, respectively. MIP was associated with approximately a 50% reduction in operating time, a sevenfold reduction in length of hospital stay, and a mean cost savings of $2,693 per procedure, which represents nearly a 50% reduction in total hospital charges.

Conclusions

A dramatic and sustained shift has occurred in the surgical treatment of primary HPTH: MIP has replaced traditional exploration for most patients.

Felix Mandl performed the first successful parathyroidectomy in Vienna in 1925.[1] The patient, Albert J., had primary hyperparathyroidism (HPTH) associated with advanced osteitis fibrosa cystica and was severely disabled. The operation was performed under local anesthesia, at which time four parathyroid glands were identified and a single enlarged gland was resected. Although the patient experienced marked resolution of his symptoms, recurrent disease occurred 6 years later and he ultimately died of uncontrolled hypercalcemia.[2]

Standard management of primary HPTH evolved to include bilateral cervical exploration, usually under general anesthesia. However, because most cases of primary HPTH are caused by a single enlarged parathyroid adenoma, several investigators have questioned the need for routine bilateral cervical exploration.[3–6] This issue has resurfaced as the quality of noninvasive preoperative imaging techniques have improved. Technetium-99m sestamibi scans, when combined with single photon emission computed tomography (SPECT), can yield accurate preoperative three-dimensional localization of enlarged parathyroid glands.[7] This allows the surgeon to plan a localized operation. In addition, the recent practicality and implementation of rapid parathyroid hormone (PTH) assays have resulted in the ability to measure PTH in the operating room, before and after tumor extraction, thereby obtaining objective evidence of the adequacy of resection.[4–6] Thus, minimally invasive parathyroidectomy (MIP) techniques have become practical and appear likely to replace conventional bilateral cervical ex-

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ploration for most patients with primary HPTH. We have previously reported our experience with the initial 100 patients who underwent MIP.[6] This single-surgeon series of 656 consecutive patients affords the opportunity to analyze changes in the surgical management of primary HPTH during the past decade.

METHODS

Stratification

Six hundred fifty-six consecutive patients with biochemically confirmed primary HPTH were explored by one surgeon between January 1990 and March 2001. Patients with secondary or tertiary HPTH were excluded from this investigation. During the initial phase of the study, conventional bilateral cervical exploration was routinely performed under general anesthesia. In all instances the surgeon attempted to identify at least four parathyroid glands and resected any enlarged glands. Beginning in March 1998, MIP was used with ever-increasing frequency. This procedure consists of preoperative localization with high-quality sestamibi scans imaged with SPECT, surgeon-administered cervical block anesthesia, limited exploration, rapid intraoperative PTH assay (Nichols Institute Diagnostics, San Juan Capistrano, CA), and same-day discharge.[6] We have recently reported the analytic performance and technical aspects of this assay.[8] Informed consent was obtained from all patients.

Data Analysis

Data were collected in a prospective database that included demographic information, symptoms, signs, serum PTH and calcium levels, imaging data, surgical technique, operative and pathologic findings, surgical and anesthetic times, conversion rates from MIP to general anesthesia, perioperative complications, length of hospital stay, total hospital charges, and immediate postoperative and long-term follow-up data. All patients were seen 7 to 10 days after surgery and in long-term follow-up, at which time serum PTH and calcium levels were obtained. The results obtained in MIP conversions were analyzed in the MIP group. One patient who underwent MIP was excluded from analysis of length of stay and total hospital charges because she presented with life-threatening pancreatitis in the setting of primary HPTH. Her prolonged hospital course was a result of her preoperative pancreatitis. Redo cases were defined as patients who had undergone previous parathyroid or thyroid exploration. Results are presented as the group mean ± SEM, unless otherwise indicated. Statistical analyses were performed with a two-tailed Student *t* test.

RESULTS

Six hundred fifty-six consecutive patients were shown to have primary HPTH, as evidenced by an elevated or inappropriate intact serum PTH level in association with hypercalcemia. There were 459 (70%) female patients and 197 (30%) male patients, with a mean age of 57.5 ± 0.5 years (range 13–93), in the entire series. Symptoms and signs of primary HPTH are listed in Table 1. There were no significant differences between patients who underwent conventional or MIP exploration with regard to age, sex distribution, symptoms and signs, or preoperative PTH or calcium levels.

Table 1. SYMPTOMS AND SIGNS OF HYPERCALCEMIA*

	Percent
Symptoms	
Fatigue	28
Mental status change	24
Depression	12
Gastrointestinal	24
Signs	
Cardiovascular	14
Nephrolithiasis	28
Bone disease	47
Pancreatitis	2
Asymptomatic	11

* Many patients had more than one symptom or sign.

These 656 patients were stratified into standard exploration or MIP groups. Stratification was based on the surgeon's recommendation and the patient's consent to undergo one or the other procedure. Randomization was not used. Four hundred one patients (61%) underwent standard bilateral cervical exploration under general anesthesia and 255 patients (39%) underwent MIP. Thirteen patients with either multiple endocrine neoplasia type 1 (n = 9) or multiple endocrine neoplasia type 2A (n = 4) were included in the standard group. No patient with multiple endocrine neoplasia was offered MIP. This stratification and the relative distribution of new versus redo cases are shown in Figure 1. The MIP technique was instituted in 1998 and in this series rapidly replaced traditional exploration for the majority of patients (Fig. 2). In addition to the relative redistribution of techniques, the magnitude of operations increased dramatically and in 2000 was 135 procedures per year. The precipitous decline in case frequency in 2001

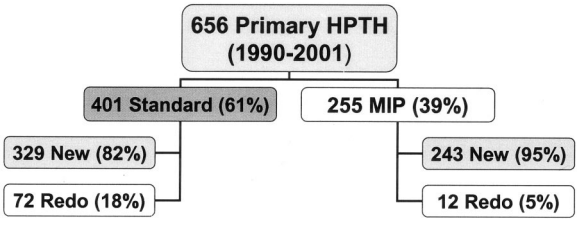

Figure 1. Flow diagram showing stratification and distribution of procedures.

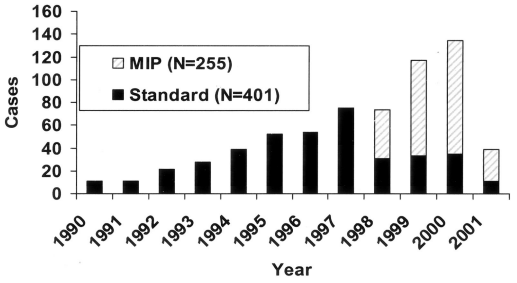

Figure 2. Sequential distribution comparing frequency of standard and minimally invasive parathyroidectomy (MIP) procedures.

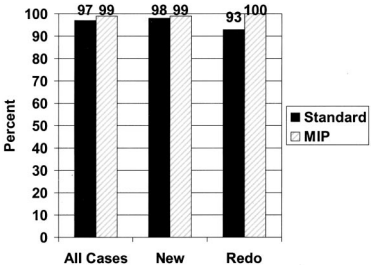

Figure 4. Cure rates comparing standard and minimally invasive parathyroidectomy (MIP) procedures, including all procedures as well as the subsets of new and redo procedures.

represents a partial year of data accumulation and the departure of the surgeon to assume a new academic position.

Sestamibi scans were obtained in 77% and 98% of patients who underwent standard and MIP explorations, respectively. As shown in Figure 3, a positive scan was obtained in 96% of patients who underwent MIP. Additional imaging studies were not routinely obtained in either group. Occasional patients with negative sestamibi scans who presented with additional imaging studies were offered MIP.

The successful outcome of surgery for primary HPTH is determined by the maintenance of eucalcemia at the arbitrarily accepted interval of 6 months after surgery. Based on this definition, the overall cure rate for the entire series was 98%. The cure rate was indistinguishable comparing the two groups, with 97% and 99% for standard and MIP explorations, respectively (Fig. 4). Subgroup analysis of the cure rate shows that favorable and indistinguishable results were obtained comparing new and redo explorations.

There were no perioperative deaths. The complication rate for the entire series was 2.3%, reflecting rates of 3.0% and 1.2% in the standard and MIP groups, respectively (Table 2). Two of the 12 complications in the standard group of 401 procedures and 1 of the 3 in the MIP group of 255 procedures occurred during remedial cervical exploration. The only complication unique to the MIP group was a seizure that resulted from lidocaine toxicity. The incidence of ipsilateral recurrent laryngeal nerve injury of 0.7% and 0.8% for standard and MIP groups, respectively, was indistinguishable.

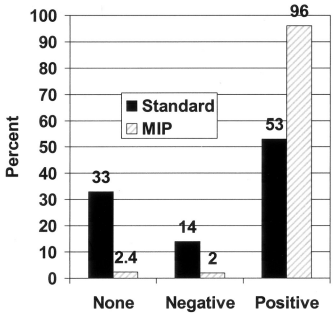

Figure 3. Results of preoperative sestamibi scans in patients who underwent standard or minimally invasive parathyroidectomy (MIP) exploration.

Two hundred twenty-six of the 255 patients (89%) who elected to undergo MIP were successfully managed with this technique. Twenty-nine patients (11%) required conversion to general anesthesia (Table 3). In all instances, conversion was performed in a standardized controlled fashion using neuromuscular blockade and endotracheal anesthesia. Eight procedures were converted to accomplish si-

Table 2. COMPLICATIONS

	n	Percent
Entire series	15/656	2.3
Standard	12/401	3.0
Ipsilateral recurrent nerve	3	0.7
Hypocalcemia	2	0.5
Atrial fibrillation	1	0.2
Deep venous thrombosis	1	0.2
Urinary retention	1	0.2
Neck hematoma	1	0.2
Neck edema	1	0.2
Cerebrovascular accident	1	0.2
Aspiration	1	0.2
MIP	3/255	1.2
Hematoma (coumadin)	1	0.8
Seizure	1	0.8
Ipsilateral recurrent nerve	1	0.8

MIP, minimally invasive parathyroidectomy. Two complications (1 recurrent nerve injury, 1 cerebrovascular accident) in the standard group occurred in redo cases. One of the complications (recurrent nerve injury) in the MIP group occurred in the redo setting. A postoperative neck hematoma occurred in an MIP patient who had been the recipient of a liver transplant and required chronic anticoagulation (coumadin).

Table 3. CONVERSIONS TO GENERAL ANESTHESIA (11%)

Indication	n
Concomitant thyroidectomy	8
Static parathyroid hormone	8
Technically difficult	6
Patient comfort	4
Parathyroid carcinoma	2
Seizure	1

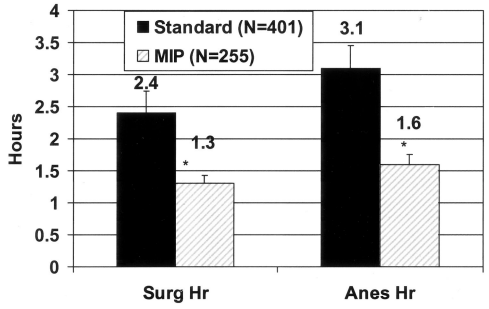

Figure 5. Length of surgery and anesthesia in hours as recorded on the anesthesia data sheet. *$P < .001$. MIP, minimally invasive parathyroidectomy.

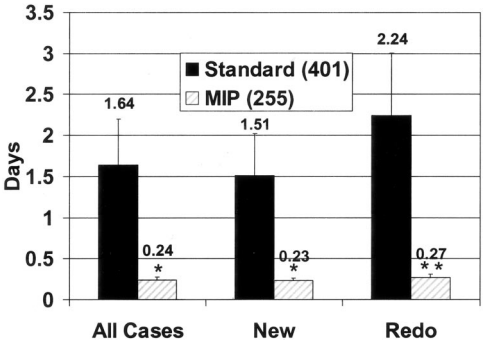

Figure 6. Length of hospital stay comparing standard and minimally invasive parathyroidectomy (MIP) procedures, including all procedures as well as the subsets of new and redo procedures. *$P < .0001$, **$P < .005$.

multaneous thyroid resections. An additional eight were converted because the intraoperative PTH level did not show at least a 50% decrease from baseline (static PTH) in spite of removing the sestamibi-identified incident parathyroid tumor. In these instances, general anesthesia expedited a formal bilateral exploration. Six additional procedures were converted because of technical difficulties, which were usually related to ensuring adequate protection of the recurrent laryngeal nerve. Four procedures were converted to optimize patient comfort, and two were converted due to the intraoperative recognition of parathyroid carcinoma and the need to perform a more aggressive resection. One patient experienced lidocaine toxicity, which resulted in a seizure; supplemental oxygen was administered and neuromuscular blockade was used to permit relatively easy control of the airway.

The durations of surgery and anesthesia are shown in Figure 5. The raw data for these intervals were obtained from anesthesia sheets and were longer than the actual incision-to-closure time recorded by the surgeon. Despite this limitation, the favorable effects on these intervals obtained with the MIP technique approximate 50% reductions in duration.

The pathologic findings presented in Table 4 show that the majority of patients in both groups had single adenomas. The weight of the parathyroid glands in the standard group (2,226 ± 746 mg) was not statistically larger than the MIP group (1,091 ± 77 mg). The incidence of double adenomas and multigland hyperplasia appeared to be higher in the standard group and may represent case selection. Two cases of parathyroid carcinoma were encountered in the MIP group. In both, enlarged parathyroid glands appeared fixed to the thyroid lobe. Accordingly, elective conversion to general anesthesia was used and the parathyroid glands were resected in continuity with the ipsilateral thyroid lobes. Permanent histology confirmed parathyroid carcinoma in both instances. Follow-up at 15 and 20 months indicated apparent cure.

Table 4. PATHOLOGY

	Standard	MIP
Single adenoma	325 (81%)	236 (92%)
Double adenoma	44 (11%)	3 (5.1%)
Hyperplasia	28 (7%)	4 (1.6%)
Carcinoma	0 (0%)	2 (0.8%)
No pathologic finding	4 (1%)	0 (0%)

MIP, minimally invasive parathyroidectomy.

The mean length of hospital stay for the MIP patients of 0.24 ± 0.06 days compared favorably to the 1.64 ± 0.14 days for patients who underwent standard exploration (Fig. 6). The median length of stay for the MIP group was zero. This favorable effect on length of stay was also upheld when the data were stratified to analyze new and redo procedures.

The financial impact of the MIP technique on total hospital charges is presented in Figure 7. The mean savings per individual MIP patient was $2,693, which represents 49% of the total hospital charge. This savings was also applicable to the new and redo procedures.

The biochemical effects of the standard and MIP techniques on serum levels of intact PTH and calcium are shown in Figures 8 and 9, respectively. The elevated preoperative

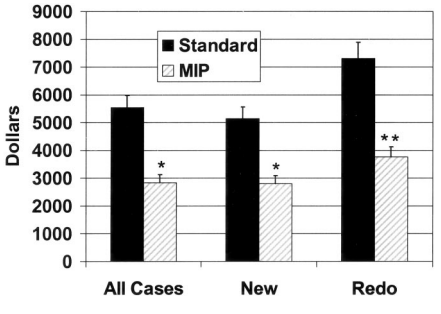

Figure 7. Total hospital charges comparing standard and minimally invasive parathyroidectomy (MIP) procedures, including all procedures as well as the subsets of new and redo procedures. *$P < .0001$, **$P < .05$.

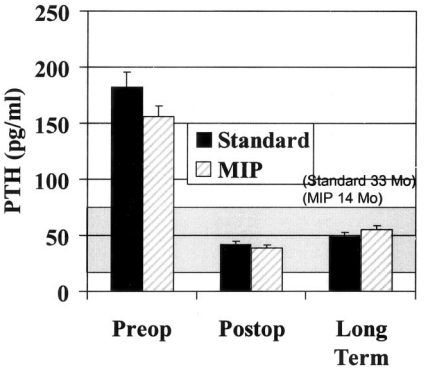

Figure 8. Serum intact parathyroid hormone levels comparing patients undergoing standard and minimally invasive parathyroidectomy (MIP) before surgery, 7 to 10 days after surgery, and after long-term follow-up. The gray area indicates the normal range for serum intact parathyroid hormone (10–72 pg/mL). The preoperative levels for both groups were substantially elevated compared with the postoperative and long-term values. However, there were no differences comparing the standard and MIP groups.

serum PTH and calcium levels returned to normal by the first postoperative visit. Importantly, the durability of both techniques is shown by long-term follow-up, with a mean follow-up of 14 and 18 months for the MIP PTH and calcium levels, respectively.

Three patients who were noted to have undergone curative resections, with a return to normal of their postoperative calcium levels for intervals that exceeded 6 months, were subsequently noted to develop recurrent disease. Two of these patients initially presented for remedial cervical exploration and were explored using standard techniques, at which time enlarged parathyroid glands were resected, and the calcium levels returned to normal. Mild recurrent disease developed at 8 and 25 months after surgery. One patient in the MIP group who underwent curative resection of an enlarged parathyroid gland, with a subsequent return to normal of his serum PTH (19 pg/mL) and calcium (9.7 mg/dL) levels, appears to have developed mild recurrent disease 19 months after surgery, with a serum PTH level of 47 pg/mL and a calcium level of 10.7 mg/dL.

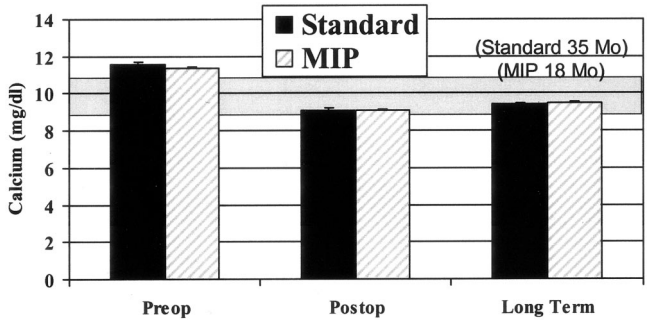

Figure 9. Serum calcium levels obtained before surgery, after surgery, and in long-term follow-up. The gray area indicates the normal range for serum calcium (8.4–10.5 mg/dL). The preoperative levels for both groups were substantially elevated compared with the postoperative and long-term values. However, there were no differences comparing the standard and minimally invasive parathyroidectomy (MIP) groups.

DISCUSSION

The treatment of choice for primary HPTH remains a carefully performed exploration by an experienced parathyroid surgeon. The exploratory technique has both been modified and reinstituted since the first successful parathyroidectomy was performed under local anesthesia by Felix Mandl 76 years ago.[1]

The increased sensitivity of parathyroid imaging allows the surgeon to plan a localized exploration designed to remove the common single focus of disease, the parathyroid adenoma. Patients with known multigland hyperplasia are not offered this technique. However, if such a patient is encountered during performance of MIP, bilateral exploration can be accomplished with this technique, or the procedure can be converted to general anesthesia. The rapid turnover of the intraoperative PTH assay yields on-site confirmation of either the adequacy of resection or biochemical data suggesting additional disease, thereby prompting additional exploration. This is an important adjunct in the operating room because sestamibi scans as well as other imaging modalities not uncommonly miss a second adenoma or fail to show multigland hyperplasia.

The intraoperative PTH assay was once considered to be expensive. However, due to ever-increasing use of the assay, we now estimate the hospital/patient charge to be approximately $150 per sample.

Parathyroid carcinoma is rare, but the surgeon must be cognizant of its presence and be prepared to perform appropriate resection of contiguous structures when it is suspected at initial presentation.

Cervical block or local anesthetic techniques are well suited for MIP, which can now be routinely performed on an outpatient basis. A superficial cervical block is ideally suited for this procedure and can be easily administered by either the surgeon or anesthesia personnel.

The success of the MIP technique is confirmed by long-term objective evidence of cure and complication rates that are at least as good as those achieved by conventional exploration. The favorable cosmetic results and ease for the patient have resulted in a preference by both the patient and referring physicians. In addition, the cost savings of approximately 50% per procedure will no doubt be viewed as a favorable attribute by the patient, third-party payers, and the global healthcare delivery system. In this series MIP has replaced traditional exploration for the majority of patients with primary HPTH who presented with de novo disease, as well as select patients who were referred for remedial cervical exploration.

Patients with “asymptomatic” primary HPTH represented a small subset of the current series (11%). There continues to be debate about the appropriate management of such individuals. The previously dated NIH consensus confer-

ence recommended that many of these patients should be managed without surgery, with careful medical follow-up.[9] It appears likely that the successful adoption of MIP will shift the recommendations of our endocrinology colleagues, some of whom now recommend referral of all patients with primary HPTH for surgical evaluation.[10] This important issue will be reviewed, and it appears likely that new guidelines will be issued during an upcoming NIH consensus conference scheduled for April 2002.

Acknowledgments

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Discussion

DR. COLLIN J. WEBER (Atlanta, GA): I rise to applaud Dr. Udelsman for a pioneering study in minimally invasive parathyroid exploration. To my mind, the challenge of minimally invasive approaches for parathyroidectomy is maintenance of the excellent outcomes expected with conventional neck exploration. Identification and effective treatment of multiglandular parathyroid disease is the crux of the issue. In our hands, neither sestamibi nor ultrasound nor any other preoperative test can completely rule out that diagnosis. It is becoming evident, however, that sestamibi plus ultrasound plus intraoperative PTH measurements are synergistic and may allow limited exploration with high success rates in a percentage of our patients.

There is a learning curve for this sort of operation, I can assure you. The key to success, I would submit, is careful patient selection preoperatively. In our unit at Emory, we recognize several contraindications to limited parathyroid exploration. These include the presence of a sizable goiter or the need to do a thyroidectomy, the identification of parathyroid carcinoma, renal cases (secondary and tertiary hyperparathyroidism), and obvious familial cases are not candidates for this procedure, in our opinion. In addition, we believe that if you do not have intraoperative PTH available to you, limited-exposure parathyroidectomy will have an unacceptably high failure rate. There are several relative contraindications, which include an unclear sestamibi or ultrasound, particularly discordance of those two tests, any evidence for or suspicion of multiglandular disease, and perhaps even the large adenoma.

I would add a word of caution about the length of follow-up. In Dr. William McGarity's experience with multiglandular disease, the first of his recurrences was at 4 years. I think that if we take that into account and select our patients as best we can to avoid exploring minimally those with multiglandular disease, this will promote progress in this field and the indications for parathyroidectomy, I believe, will expand, for example to the normal-calcium, elevated-PTH patients.

DR. RICHARD E. GOLDSTEIN (Nashville, TN): The data from this manuscript demonstrate that a scan-directed minimally invasive technique under local anesthesia is as effective—and I will go ahead and make that statement—is as effective as the standard bilateral approaches that we have all learned. This technique applies to patients in whom the single parathyroid adenoma can be identified preoperatively. Current data suggests that 80% to 90% of patients with primary hyperparathyroidism, have pathophysiology attributable to a single adenoma, that they will have positive parathyroid scans approximately 80% to 90% of the time. Given this background, a high percentage of patients with primary hyperparathyroidism are eligible for a procedure such as minimally invasive parathyroidectomy and are cured.

Dr. Udelsman has demonstrated that the procedure incurs less hospital charges than standard bilateral approaches under general anesthesia. I commend Dr. Udelsman on his results. I do have several questions and ask him to comment on these.

The first one really deals with the use of the parathyroid hormone assay. Your form of minimally invasive parathyroidectomy uses the intraoperative parathyroid hormone measurement that has been strongly driven, as you point out, by the work of another member of the Southern Surgical Association, Dr. George Irvin. This assay adds some cost to the procedure, but I really ask how much this assay has in fact helped you. I note that eight patients out of your series were converted to bilateral procedures due to the failure of the PTH level to fall by at least 50%. What was found in these eight patients? While a failure of the PTH level to fall by at least 50% can mean that there is a double adenoma or four-gland hyperplasia, there have also been false-positives. And I actually believe there was at least one paper pointing that out by another member who just spoke, Dr. Weber.

One of the reasons I am dealing with this is, I think it was you, Dr. Udelsman, who, at the last meeting of the American Association of Endocrine Surgeons, took an informal hand-raising poll of the members to ask how many of them used this assay as part of their standard approach, and approximately 40% of the surgeons in the room raised their hand. So I think we are starting to hover on the issue of whether the use of intraoperative parathyroid hormone assay is becoming the standard of care. And I ask you to comment on that. I wonder if you might also comment on which commercial set-up you now use and what the cost is.

My last question deals a little bit with the reoperative group, of which you had 12 patients, or 5%, in the MIP group. First, what is the role of MIP in this setting? It looks from the data as if you are sending these patients home also on the same day. At least with some of the patients that we have seen, there is certainly a concern about whether the other parathyroids are still present when one is reoperating. And I wonder if you might comment on your approach to keeping these patients versus sending them home on the same day.

Again, I would like to thank you for asking me to comment on this paper. I think it is excellent.

DR. SAMUEL A. WELLS, JR. (Durham, NC): Dr. Udelsman reports one of

the largest personal experiences in patients with primary hyperparathyroidism, and his success rate of 98% is extraordinary. This is especially impressive in view of the fact that "double adenomas" or hyperplasia were present in 18% and 6.7% of patients having either a standard procedure or minimally invasive parathyroidectomy (MIP), and 13% of the patients had remedial operations for persistent or recurrent hyperparathyroidism after a failed initial operation. It was not mentioned whether patients with hyperparathyroidism due to MEN 1, MEN 2A, or familial hypocalciuric hyperparathyroidism were excluded. A successful operation was based on the documentation of normal serum calcium and PTH levels at 6 months following surgery. This is perhaps too soon to determine outcome, as recurrent hyperparathyroidism may not be evident until several months or years after parathyroidectomy.

There are no data regarding serum calcium levels or PTH; rather, the success rates for all patients in the standard and MIP groups are shown. One can portray large data sets, such as in those from this study, in a scattergram, where the most recent peak serum calcium level is shown as a point on the ordinate as a function of time on the abscissa. Further clarity can be given if the upper and lower levels of the PTH values are shaded on the scattergram, assuming that the same assay was used for all patients.

The MIP technique is relatively new; thus, practicing surgeons did not learn the procedure during surgical residency. How should such a procedure be taught to practicing surgeons? The lack of an effective postgraduate education curriculum is a major issue in surgery, as alluded to by Dr. Britt in his presidential address this morning. There is no FDA for surgery, and any of us can devise an operative procedure and introduce it into clinical practice, even without approval of a local IRB. It is important that we develop methods of teaching surgeons how to perform new operations or to use new technology whereby technical proficiency is assured before the surgeon introduces a procedure into clinic practice.

My final point relates to the introduction of new pharmaceutical agents reported to compete for binding with the PTH receptor, thereby reducing the serum calcium level to normal in patients with hyperparathyroidism. Will these medicines obviate the need for surgery, or will there always be a place for operative intervention in patients with primary hyperparathyroidism? The remarkable success with MIP surgery, as reported by Dr. Udelsman, should assure the primacy of operative intervention in patients with this common disease.

DR. LORING W. RUE, III (Birmingham, AL): Your data suggest that there were a few patients, a small number, that underwent the minimally invasive procedure without preoperative sestamibi localization. How did you decide what side of the neck to start in? Did you use ultrasound or the navigator probe with preoperatively administered sestamibi?

DR. MICHAEL ROE (Chattanooga, TN): I enjoyed your paper very much. I think I interpreted your data from the slides correctly. It looked like 53% of your patients who underwent a standard procedure had a positive sestamibi scan. If that is true, why did they not undergo MIP? This brings up the question, who orders the sestamibi scan? Is that ordered once they see the surgeon? Or is it ordered by the referring physician—which is sort of worrisome, because occasionally there are going to be patients who clearly have the disease but they may have a negative scan, and many of those patients will not get the opportunity to see a surgeon.

The other thing that I had a question about was the MIP conversions. It didn't appear as though any were listed due to a false-positive sestamibi scan, where one goes into a spot and a diseased gland is not found in that location. Is the positive predictive value of the sestamibi scan now that good?

DR. ROGER R. PERRY (Norfolk, VA): Some groups have described the so-called 20% rule, whereby if your excised gland has greater than 20% activity compared to background, then you can terminate the procedure. Can you describe your view of the usefulness of the 20% rule?

DR. ROBERT UDELSMAN (New Haven, CT): I would like to thank the discussants for those interesting comments and answer them sequentially.

First, Dr. Weber mentioned contraindications. I agree with Dr. Weber: there are relative and absolute contraindications. I agree with his slide with only one exception, in that I don't consider thyroid disease as necessarily a contraindication, as I am willing to perform thyroid resections utilizing the same anesthetic technique.

Long-term follow-up is essential. And I agree with both you and Dr. Wells, of course, that this is the real crux of the matter. Dr. Irvin's long-term data and mine are almost analogous as to long-term results. I remind everyone, though, that just because you do a standard operation doesn't mean that the patients are not subject to long-term recurrence. There are long-term recurrences no matter how you do the operation.

Dr. Goldstein mentioned several aspects of the operation. He talked about false-positive studies and false-positive assays. False-positive studies are a problem. They are rare, but they do occur. Is it possible that you remove the abnormal parathyroid gland and the assay never falls? You persist and keep looking and looking until you can't look any more. The answer is yes, it has happened to me once, and it is a problem. The point I want to make is that neither an assay nor a sestamibi scan will ever replace clinical judgment.

What about asserting that the assay represents the standard of care? Well, it comes down to a critical question: are you willing to fail? If you are willing to fail in this operation 3% to 5% of the time because you don't find a second lesion, then don't use the assay. You will have to go back another day to complete the operation, but I don't find that irresponsible. I don't think it is fair to say if you don't have this assay you can't do the operation. But I don't want to fail 3% to 5% of the time, so I don't want to do the operation without an assay. I want to cure every patient every time.

I was asked about what the assay was. I use the Nichols assay. I have no proprietary interest in Nichols. It is a good assay. The turnover time is 12 minutes. When they initially brought that assay to us it was extraordinarily expensive. The cost has dropped dramatically. There is competition out there, which is healthy, and the assay costs will continue to come down.

Can you use this technique for a reoperation? The answer is yes, in highly select patients. It depends what they have. If they come in with a positive sestamibi scan and you read the operative note and the surgeon never explored the retroesophageal plane, and there it is in three-dimensional reconstruction demonstrating an enlarged parathyroid gland in the retroesophageal plane, that is a slam-dunk. You can do that operation in 20 minutes. So the answer is, it depends. It depends on what you see on the scan and whether you think it is going to be easy. If it is going to be difficult and the patient has a cord paralysis, that is a different patient.

Dr. Wells makes many points. And Dr. Wells, probably no one in the room knows more about this than you do.

The first question is, do I see a high incidence of multigland disease or double adenomas? The answer is, I do. And it is because I look hard. I am not sure in the standard group that every gland that I took out because it was macroscopically enlarged would have hyperfunctioned. In fact, now with MIP techniques, I may leave behind a macroscopically enlarged gland that is not hyperfunctional as proven by the PTH assay.

MEN patients should never be explored with this technique. Both MEN 1 and 2A patients have multigland disease, although it may be asymmetric. In this series there were nine patients with MEN 1, four patients with MEN 2A, all of whom had standard operations, all of whom also had thymectomies, all of whom I would do under standard techniques. I would never offer this technique for that population or the renal failure secondary hyperparathyroidism patient.

As far as plotting data on a scattergram, I appreciate it. It is a wonderful comment.

Education. One of our primary missions is to train, and this operation is a problem for education. I think it is better to train faculty and residents and students using standard techniques. They can see the anatomy better. They can see all of the glands. I haven't resolved how to solve this problem. Surgeons are not ready for this operation until they know how to do a standard operation, and if you only learn this operation, you will never be a good parathyroid surgeon. We are struggling with that problem. I don't have an easy answer for it.

About training our colleagues, I think the College can help us. I just made a movie for the College. That is one technique. The other is the spirit of this conference. We are collegial. You are all invited to New Haven and I will show you the operation anytime you want to see it.

I also want to mention an important point that was referred to: does this change the indications for surgery, especially in asymptomatic patients? Maybe it does. There is nothing our medical colleagues would like more, Dr. Wells, than to have a medicine so these patients never need surgery. And they are going to work from now until forever and maybe some day they will have it and maybe we will be out of business. And that is just fine. If that is better for the patient, I will support it. But right now there is no such receptor antagonist or agonist, and we will continue to operate.

There is an NIH conference coming up in April, a consensus conference for the management of primary hyperparathyroidism. I am going to be there to suggest that every patient with primary hyperparathyroidism at least deserves a referral to a surgeon to discuss this as an option for treatment.

There are many other comments Dr. Rowe mentions. What do you do with patients with negative sestamibi scans? Patients are often referred with multiple studies, CTs, MRIs, sonograms. If I have one and it is positive, I am willing to accept it and operate based on it. Dr. Rowe noted that 50% of my patients had sestamibi scans in the standard group. That is because I started doing sestamibi scans before the MIP technique was available. Virtually all of those patients now would be offered the technique at this time.

What about MIP conversions? Conversions are always going to happen. Did I ever have a false-positive sestamibi scan? Of course I did. Sestamibi uptake is not limited to the parathyroid gland. Any tissue that has a large amount of mitochondria, such as a thyroid adenoma or a Hurthle cell or follicular lesion, will light up with sestamibi. The surgeon has to know that.

The last question was about background-to-tumor ratios. The question implies using an intraoperative gamma probe, which I do not use. I find that high-quality sestamibi scans with 3D reconstruction give incredible information, and I don't find the probe necessary.